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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/312,351	05/14/1999	JON A. WOLFF	MIRUS.006	2480
25032	7590	08/23/2005	EXAMINER	
MIRUS CORPORATION 505 SOUTH ROSA RD MADISON, WI 53719			WOITACH, JOSEPH T	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/312,351	WOLFF ET AL.
	Examiner Joseph T. Woitach	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 27 May 2005.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 7-11 and 19-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 7-11 and 19-28 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: \_\_\_\_\_

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 27, 2005 has been entered.

**DETAILED ACTION**

This application claims benefit to provisional application 60/085,764, filed May 16, 1998.

Applicants' amendment filed May 27, 2005 has been received and entered. Claims 1-6, 12-18 have been canceled. Claims 7, 19 and 24 have been amended. Claims 7-11, 19-28 are pending and currently under examination.

***Specification***

The statement filed May 27, 2005 regarding the sequence listing and CFR has been received and entered. The nucleotide sequence disclosure contained in this application complies with 37 CFR 1.821-1.825.

It is noted that the specification should be amended to reflect a SEQ ID NO: for the given sequence. For example page 54, line18, should be amended to have SEQ ID NO: 1 associated with the poly-glutamic acid recited.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-11, 24-28 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

The amendment to the claims have addressed the previous basis of rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-28 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that the terminology is well known as evidenced by citation of several relevant references (page 5), and given the knowledge in the art, one of skill would readily know how to construct a compound containing a disulfide that is subject to intermolecular attack (pages 5-6). See Applicants' amendment, pages 5-6. Applicants' arguments have been fully considered, but not found persuasive.

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The basis of the rejection is a new matter rejection, and addresses whether the instant specification specifically contemplates the claimed invention. In this case, applicants have not pointed to literal support, and as indicated previously a review of the specification by the examiner can not identify literal support for such a limitation. Importantly, none of the possible R groups disclosed provide for a structure with a third thiol group. Examiner does not contest that such groups and/or interactions can exist as evidenced by Applicants' citations, rather these are not contemplated by the teachings of the instant specification.

Again, 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Claim 24 has been amended to recite "is activated by intramolecular attack from a free thiol such that it is cleaved more rapidly than oxidized glutathione", clearly implying that the third thiol group is comprised on the claimed compound, owerer as indicated previously, there is no literal nor structural support for such a compound. None of the potential R groups taught recite a third sulphydryl group is contemplated. Moreover, there is no teaching for providing a compound with the particular property claimed where three thiol groups are present.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 24-28 stand also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. Again, while similar compounds are known in the art, they are not presented as instantly claimed. As noted previously, there is no specific description nor guidance

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to what this phrase encompasses, nor how to generate this compound. Further, if a third thiol group existed in the composition for intramolecular attack that would result in a rapid cleavage of a disulfide bond, it is unclear how such a chemical would be made or exist in light of this property.

For the reasons above and of record, the rejection is maintained.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-11, 19-28 stand rejected under 35 U.S.C. 102(b) as being anticipated by Pierce catalog as evidenced by Arpicco *et al.*

Independent claims 7, 19 and 24 have been amended to encompass a “composition containing a labile disulfide bond”, and set forth a method for producing the composition. However, while the method steps are active “forming” steps, a reasonable interpretation of the breadth of the claims is that the composition must simply comprise the labile disulfide. While the claim is set forth as a product by process, the breadth of the claim for what a reactive group is, the requirement for its presence in the final product, and now the claims have been amended to indicate that the molecule is formed with “separate molecules”, no longer requiring that the resulting compound be different at each end. The present specification teaches how to make cross-linking compounds with the recited functional limitation. The broadest reasonable

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interpretation of the invention as instantly claimed appears to be a homo-bi-functional cross-linker or hetero-bi-functional cross-linker.

As stated previously, assessing what is required and encompassed by the present independent claims it appears that all that is required is a compound with a di-sulfide bond that is cleaved more rapidly than oxidized glutathione. The exact nature of the chemical composition on either side of the di-sulfide bond is broad, but is being interpreted to encompass at least anything that does not affect the ability of the di-sulfide bond to be cleaved more rapidly than glutathione. Claims 24-28 are included in the basis of the rejection because while they appear to require a the presence of a third sulphydryl group it is unclear when it was present or if it has to be present in the final product since it was "activated" (claim 24).

The Pierce catalog discloses multiple bi-functional and hetero-bi-functional cross linkers that contain disulfide bonds (pages T-157-T-200). As evidence by Arpicco *et al.* the disulfide bonds of these compounds are more labile and are cleaved more rapidly than glutathione. In light of the minimum requirement that the claimed composition must have a di-sulfide bond that is cleaved more rapidly than glutathione and any other chemical on either side that does not affect this cleavage rate, the hetero-bi-functional cross-linkers anticipate the claims. Since the compounds disclosed by Pierce were synthesized, and thus imply reactable groups were present, they meet the limitations of the claim to encompass reacted groups. To the extent that the composition still has reactive groups, it is noted that the cross-linkers in Pierce are sold for use in cross-linking additional molecules and maintain different reactive groups on either side of the di-sulfide bond. Again, because the linker was synthesized the presence of the reactive groups implies that other reactive groups were present/used in the synthesis of the final product.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

*Joe Woitach*  
*AU1632*